

REMARKS**I. Detailed Action****A. Status of Application**

Applicants acknowledge claim 21 is cancelled.

B. Response to Arguments

(1) Applicants acknowledge the Examiner's withdrawal of the rejection under 35 U.S.C. § 102(b) in light of Applicant's amendments and arguments.

(2) Applicants further acknowledge the Examiner's withdrawal of the objection under 37 C.F.R. § 1.56 in considering patentability of the claims under 35 U.S.C. § 103(a).

II. Claim Rejections – 35 U.S.C. § 103(a)

Claims 1, 3-17 and 26-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hu et al. (U.S. Patent No: 6,203,984) in view of Li et al. (U.S. Patent No: 6,399,334). The Examiner notes "specific motivation is provided by the teachings of Hu et al. and Li et al. to improve sensitivity of the assay. An ordinary practitioner would have been motivated to combine the teachings of Hu et al. with the method of Li et al. to achieve a sensitive method of the amplifying cDNA by incorporating the reverse transcriptase RNase H⁺ because this limitation would improve the elimination or reduce background contamination."

Applicants respectfully traverse this rejection. The test under § 103(a) is whether the differences between the prior art and the invention, as a whole, would have been obvious to one having ordinary skill in the art. *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 662 (Fed. Cir. 2000). The prior art must teach one of ordinary skill in the art to combine elements from the prior art in the manner combined by the inventor. *Crown Operations Int'l, Ltd. v. Solutia, Inc.*, 289 F.3d 1367, 1376 (Fed. Cir. 2002). Thus, obviousness can not be determined by a hindsight gathering

of elements in order to "fit the parameters" of the invention. *ATD Corp. v. Lydall, Inc.* 159 F.3d 534, 546 (Fed. Cir. 1998).

Hu et al. teach a method of amplifying cDNA which contains the steps of obtaining an mRNA, reverse transcribing the mRNA into cDNA with reverse transcriptase to form a cDNA-mRNA complex, degrading the mRNA from the complex to form a linear cDNA, ligating the ends of the linear cDNA to form a circular cDNA, and introducing a first and second primer, which is then followed by an amplification of the cDNA using primer extension amplification.

Applicants have amended the claims to indicate that the sequence specific PCR primers are designed such that one primer has a 3' end toward the 3' end of the circular cDNA and that the other primer has a 3' end toward the 5' end of the circular cDNA. This is an important aspect of the invention. As taught by the specification: "[t]he design of the first and second primers differs from that of traditional PCR of cDNA first in that using a single nucleic acid strand as a template. The primers are instead designed so that each one has a 3' end of the primer which is toward either the 5' or 3' end of the polynucleotide. This means that the forward primer will typically be toward the 3' end of the molecule and the reverse primer will be towards the 5' end of the molecule." A primer extension procedure may then be used to re-amplify the resulting nucleotide sequence such that the end product will include both the 3' and 5' ends of the cDNA outside of the primers.

The Hu reference makes no mention that the PCR primers are designed so as to have this feature. Instead, the reference only describes primers which are oriented in a single direction. (See, e.g., column 2, lines 5-9 and column 9, lines 10-14). Therefore Applicants submit that claims 1, 3-17 and 26-27 are clearly not obvious under Hu *et al.* because it does not teach one of ordinary skill in the art to combine elements so as to come out with a method for amplifying

polynucleotide sequences using specific PCR primers which are oriented such that one primer has its 3' end towards the 3' end of the circular cDNA and the other has its 3' end toward the circular cDNA's 5' end.

III. Conclusion

In light of the above amendments and remarks, Applicants respectfully assert that claims 1, 3-17 and 26-27 are now in condition for allowance. Applicants respectfully request reconsideration and withdrawal of the above rejections. If it is felt that it would aid in prosecution, the Examiner is invited to contact the undersigned at the number indicated to discuss any outstanding issues.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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